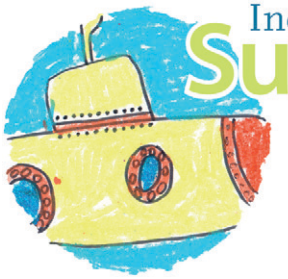

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4 An Infant with Status Epilepticus and Stroke

Firdhous Alimathunisa Abdul Kather, MD,* Kallol Kumar Set, MD*

*Division of Pediatric Neurology, Children's Hospital of Michigan, Detroit, MI

PRESENTATION

A 33-day-old boy is admitted to the hospital with seizure episodes. The antenatal course was complicated by gestational diabetes mellitus and group B streptococcus (GBS) urinary tract infection for which the mother received intrapartum antibiotic drug therapy. The patient was born at term by induced vaginal delivery because of prolonged rupture of membrane but with Apgar scores of 8, 9, and 9 at 1, 5, and 10 minutes, respectively, without any birth asphyxia, meconium aspiration, and nuchal cord. On the day of admission, the patient started having tonic-clonic movement involving the left upper extremity associated with left arm extension, fisting of the left hand with squeezing movement, and eye deviation to the left associated with grunting. He continues to have seizures until he is given 4 doses of intravenous lorazepam 0.1 mg/kg, a loading dose of levetiracetam 20 mg/kg intravenously, and phenobarbital 20 mg/kg intravenously. He also presents with fever (rectal temperature of 102.9°F [39.4°C]), which is treated with 10 mg/kg of rectal acetaminophen twice.

On examination, peripheral capillary refill is 3 seconds. He has no spontaneous eye opening but is responding to painful stimuli. The anterior fontanelle is bulging, and pupils are 2 mm and reacting normally. Funduscopic examination did not show retinal hemorrhage, but optic disc margins were not clear bilaterally. Movement is diminished overall, but no movement of the left upper and lower extremities is present. The Moro reflex is incomplete, but rooting and sucking reflexes are present. Four beats of ankle clonus are present bilaterally. Initial laboratory evaluation demonstrates a C-reactive protein level of 1.57 mg/L (14.9 nmol/L) (reference range, <9.10 mg/L [<86.7 nmol/L]), a calcium level of 8.4 mg/dL (2.1 mmol/L), capillary blood pH 7.35 with P_{CO_2} of 38 mm Hg, and a lactate level of 18 mg/dL (2 mmol/L). A complete blood cell count reveals a total white blood cell count of 2,100/μL (2.1×10^9/L), with 33% lymphocytes and 49% neutrophils, and Gram-positive cocci are found in the blood.

DISCUSSION

The cerebrospinal fluid (CSF) findings showed a red blood cell count of 24/μL (0.000024×10^{12}/L), a white blood cell count of 66/μL (0.066×10^9/L) (neutrophils 93%, monocytes 1%), a glucose level of 17 mg/dL (0.94 mmol/L), a protein level of 0.22 g/dL (2.2 g/L), and gram-positive cocci, suggestive of bacterial meningitis.

AUTHOR DISCLOSURE Drs Abdul Kather and Set have disclosed no financial relationships relevant to this article. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device. Dr Set's current affiliation is Division of Pediatric Neurology, Dayton Children's Hospital, Dayton, OH.

Clinical Course and Management

The patient was started on broad spectrum antibiotic drug therapy because there were concerns for meningitis. Head ultrasonography showed bilateral subdural effusions consistent with bacterial meningitis. An electroencephalogram showed diffuse neuronal dysfunction and focal seizures from the right central parietal region.

Magnetic resonance imaging (MRI) performed on day 2 showed a right posterior frontal anterior parietal acute infarct involving the precentral and postcentral gyrus (Fig 1). Also, there was multifocal loculated diffusion restriction, likely a collection of pus or small subdural empyema around the frontal and parietal convexity more on the right side, fitting the clinical presentation (Fig 2). Contrast-enhanced MRI of the brain showed leptomeningeal enhancement consistent with meningitis (Fig 3). There were no visible retinal hemorrhages found in gradient echo MRI; therefore, suspicion of child abuse was low, but it was included in the differential diagnosis initially. Also, a dilated eye examination did not show retinal hemorrhage.

The patient had a prolonged episode of seizure progressing to status epilepticus. He was started on a midazolam drip (continued for 5 days) with an increased dose of levetiracetam (60 mg/kg per day) and phenobarbital (5 mg/kg per day). The culture returned positive for *Streptococcus agalactiae* sensitive to ampicillin. A central venous catheter was placed, and ampicillin therapy was continued. Clinically, the patient stopped having seizures, and the weakness of the left upper extremity improved. MRI, electroencephalography, and lumbar puncture were repeated on day 29 (Figs 1–3).

On day 29, MRI showed cystic encephalomalacic changes in the right parietal lobe with the resolution of extra-axial diffusion restriction and substantial improvement of leptomeningeal enhancement (Fig 3). CSF continued to show 26 nucleated cells, 59% neutrophils. CSF culture showed no growth. After 33 days of ampicillin therapy, the central line was removed and the patient was discharged on oral levetiracetam and phenobarbital.

Final Diagnosis

The infant was diagnosed as having severe late-onset bacterial GBS meningitis with acute stroke, subdural empyema, and status epilepticus.

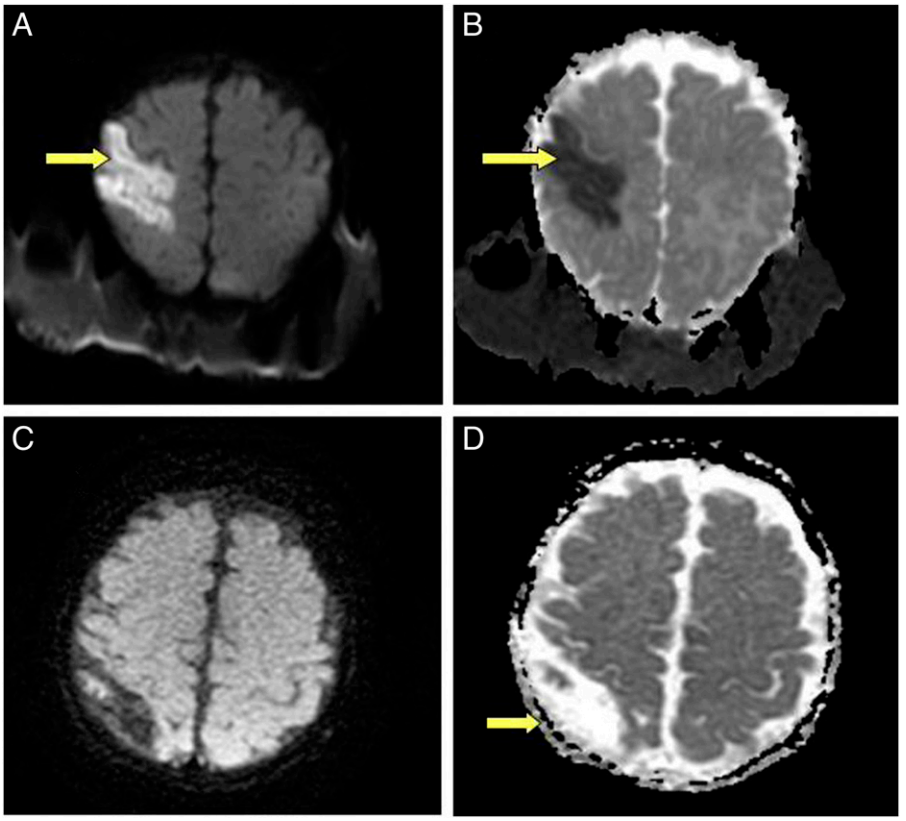

Figure 1. Magnetic resonance imaging of the brain. A and B. Diffusion-weighted image and apparent diffusion coefficient image demonstrate a focal, parenchymal, somewhat wedge-shaped diffusion restriction (yellow arrows) along the right precentral and postcentral gyrus. C and D. There is no diffusion restriction after treatment, but encephalomalacic changes (yellow arrow) are noted.

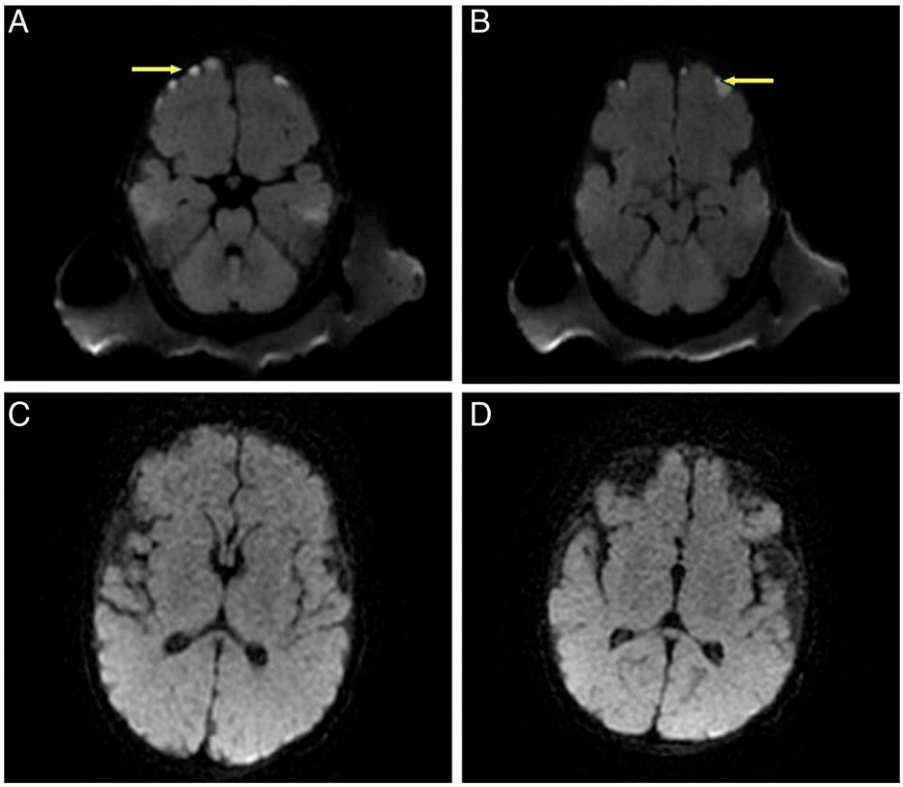

Figure 2. Magnetic resonance imaging of the brain. A and B. Multifocal small diffusion restriction (yellow arrows) along the frontal and parietal convexity is more prompt on the right side, raising the possibility of subdural empyema. C and D. The restriction disappeared after treatment.

The Condition

Bacterial meningitis is a pia-arachnoid infection and an inflammatory response in the CSF. It is a common manifestation of late-onset (day 7–89 after birth) neonatal sepsis. It occurs in 25% of neonates with bacteremia, with an incidence ranging from 0.25 to 1 per 1,000 live births. In developed countries, bacterial meningitis is commonly caused by GBS serotype III, accounting for 50% to 78% of all cases. Late-onset infections suggest nosocomial or community acquisition, or perinatal transmission from human milk, although the maternal flora colonizing the neonate may still be a source of infection.

Universal screening of pregnant women in the United States for rectovaginal GBS colonization at 35 to 37 weeks' gestation and administration of intrapartum antimicrobial prophylaxis to carriers has reduced the incidence of early-onset

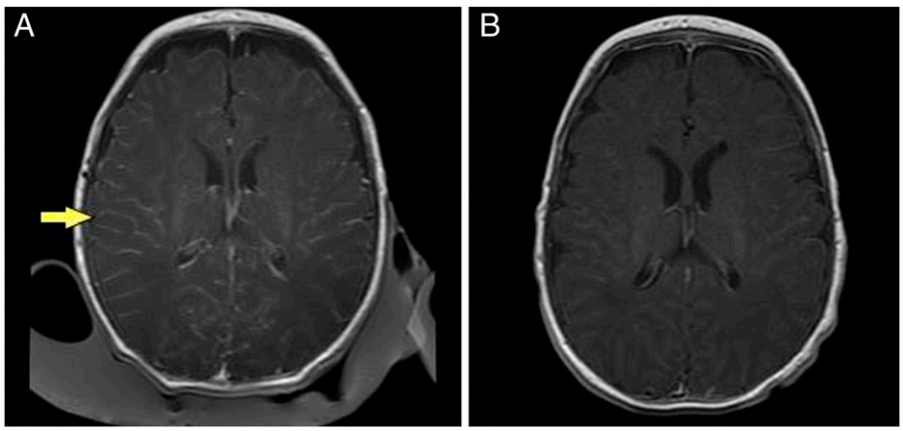

Figure 3. Magnetic resonance imaging of the brain. A. Leptomeningeal enhancement (yellow arrow) is seen after gadolinium administration. B. Enhancement disappears after treatment.

disease, but the incidence of late-onset disease has remained stable at an average of 0.34 per 1,000 live births in the United States.

GBS infection presents with symptoms such as fever (81%), irritability/crying (42%), and poor feeding (39%). Twenty percent to 50% of infants with meningitis present with seizures. Up to 50% of infants with a history of meningitis will be neurologically impaired, and 25% will have a severe disability. Meningitis is a very rare cause (~3%) of arterial ischemic stroke in children. Hernández et al showed that the penetrating lenticulostriate and thalamostriate arteries, which supply the basal ganglia, thalamus, and deep white matter, are mostly affected (88%), and superficial cortical infarction was observed in 75% of patients.

Common neurologic complications of meningitis include ventriculitis (20%), cerebral edema and increased intracranial pressure (78%), seizures (17%–40%), cerebral infarction (30%–50%), subdural effusion or empyema (7%–33%), hydrocephalus (24%), hearing loss (7%–12%), intellectual disability (4%), and developmental delay (25%).The uncommon neurologic complications of meningitis are spinal cord ischemia, brain abscesses, aneurysm formation of focal intracranial vessels, and cortical visual loss.

Eight percent to 33% of infants with bacterial meningitis have accumulation of extra-axial fluid or subdural collection of pus. This may, in turn, become an empyema, which is present in up to 1% of affected patients. If not treated early and properly, this may require surgical drainage.

Empirical therapy of possible neonatal meningitis should include intravenous ampicillin (300 mg/kg per day) or cefotaxime plus gentamicin (4–5 mg/kg per day). Once GBS have been identified and the susceptibility verified, penicillin G (450,000–500,000 U/kg per day) can be used to complete therapy for a minimum of 14 days and should be extended to 21 days or longer if complicated. Seizures are controlled with first-line antiepileptic drugs such as lorazepam, diazepam, phenobarbital, phenytoin (older babies), and levetiracetam for 1 week up to 12 months after the last seizure, and patients should regularly follow up with a neurologist.

Lessons for the Clinician

- Despite recent advances in neonatal intensive care, rapid diagnosis, and treatment, neonatal bacterial meningitis is one of the most common causes of neurologic disability.
- Despite prophylactic intrapartum antibiotic drug therapy, late-onset group B streptococcus infections in infants continue to occur and are associated with higher morbidity than are early-onset infections.
- High clinical suspicion, early diagnosis, immediate institution of therapy, and early recognition and management of complications can decrease the mortality rate and result in a better neurologic outcome.
- Subdural effusions could have been from shaking, and the stress of abuse can lead to group B streptococcus infection. Severe shaking can also cause a brain infarct and fever. So, a dilated retinal examination, magnetic resonance imaging of the eye with gradient-recalled echo sequence, or a skeletal survey is needed to exclude child abuse/inflicted brain injury.

Suggested Readings for this article are at http://pedsinreview.aappublications.org/content/40/8/431.

Suggested Readings

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Case 4: An Infant with Status Epilepticus and Stroke

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